

(FILE 'HOME' ENTERED AT 11:08:25 ON 08 NOV 2002)

FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, EMBASE, BIOSIS, MEDICONF' ENTERED AT 11:11:21 ON 08 NOV 2002

L1 102283 S CYTOCHROME (L) P450  
L2 568 S L1 AND (ENCAPSUL? OR CAPSULE OR MICROCAPSUL? OR NANOSPHERE OR  
L3 80 S L2 AND (CANCER OR TUMOR OR TUMOUR OR NEOPLAS?)  
L4 46 DUP REM L3 (34 DUPLICATES REMOVED)  
L5 46 FOCUS L4 1-  
L6 46 SORT L4 PY  
L7 13 S L4 AND PY<=1997  
L8 13 SORT L7 PY  
L9 13 S L6 AND GUNZBURG?/AU  
L10 13 SORT L9 PY

=> d an ti so au ab l10 13

L10 ANSWER 13 OF 13 SCISEARCH COPYRIGHT 2002 ISI (R)

AN 2002:503718 SCISEARCH

TI Microencapsulated, CYP2B1-transfected cells activating ifosfamide at the site of the **tumor**: the magic bullets of the 21st century

SO CANCER CHEMOTHERAPY AND PHARMACOLOGY, (MAY 2002) Vol. 49, Supp. [1], pp. S21-S24.

Publisher: SPRINGER-VERLAG, 175 FIFTH AVE, NEW YORK, NY 10010 USA.

ISSN: 0344-5704.

AU Lohr M (Reprint); Hummel F; Faulmann G; Ringel J; Saller R; Hain J; **Gunzburg W H**; Salmons B

AB Background: Conventional chemotherapy of pancreatic carcinoma is only marginally effective. This is in part due to the severity of side effects following systemic administration of the cytostatic drug. The aim was to create a therapeutic tool allowing the targeting of the conversion site of a cytotoxic prodrug to the site of the **tumor**. This was realized by transfection of the CYP2B1 gene, the major ifosfamide-converting P450 enzyme, in cells with subsequent microencapsulation and administration of these **microcapsules** to or into the **tumor**. The enzyme activity (resorufin assay) remained stable for weeks in vitro and in vivo within the microencapsulated CYP2B1-expressing cells. We demonstrated a significant antitumor effect of the intratumorally injected **capsules** against xenotransplanted human pancreatic carcinomas in the nude mouse. Angiographic experiments in the pig confirmed the feasibility of an intraarterial placement of the **capsules** into the pancreas. A clinical protocol was established and approved. Patients, material and methods: L293 cells were transfected with the CYP2B1 gene, **micro-encapsulated** (diameter 0.7 mm) under GCP conditions and packed sterile. Patients with confirmed inoperable adenocarcinoma of the pancreas underwent angiography, and **capsules** were injected into a vessel leading into the **tumor**. The patients were monitored for 48 h to exclude allergic reactions or pancreatitis. A day later, ifosfamide was administered for three consecutive days to be repeated on days 21-23. The patients were followed up for 5 months. Results: A total of 17 patients were enrolled. The patients tolerated the procedure without any complications. No allergic reactions or pancreatitis were encountered. Chemotherapy was uneventful. All patients had stable disease, and two patients a partial remission. The median survival was 44 weeks which compared favorably with that of a historical control group (22 weeks). Conclusions: The intraarterial administration of **microcapsules** for targeted chemotherapy was well tolerated. Control of local **tumor** growth was achieved.